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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,252	12/04/2000	Donald G. Munroe	P108074-0000	4192

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EXAMINER
KEMMERER, ELIZABETH

ART UNIT	PAPER NUMBER
1646	17

DATE MAILED: 09/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/581,252	MUNROE ET AL.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *17 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 December 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

Applicant's election of Group I, claims 1-16, 18 and 19, in Paper No. 16 (11 July 2003) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 17 and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 16.

Status of Application, Amendments, And/Or Claims

The amendment filed 22 January 2003 (Paper No. 14) has been entered in full. Claims 17 and 20 are withdrawn from consideration. Claims 1-16, 18 and 19 are under examination.

Sequence Rules

The instant application fails to comply with the sequence rules, 37 CFR 1.821-1.825, because each disclosure of a sequence encompassed by the definitions set forth in the rules is not accompanied by the required reference to the relevant sequence identifier. Figure 5B discloses two sequences without reference to sequence identifiers. The sequence identifiers provided for Figure 5A appear to be incorrect, and do not agree with the sequence identifiers provided for the preceding figures. Also, note that

the clean copy of the brief description of figure 5A does not match the marked up copy. Compliance with the sequence rules is required.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16, 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "biologically active fragment" recited in the claims is indefinite, since neither the specification nor the art provides an unambiguous definition for the term. Is "biological activity" limited to LPA binding, or does it encompass diverse biological activities such as immunogenicity or even nutritional activity?

The term "stringent conditions" recited in the claims is indefinite since neither the specification nor the art provides an unambiguous definition of the type of conditions encompassed by the term and the type of conditions excluded by the term.

In claims 16, 18 and 19, the preamble indicates that a ligand or antagonist is to be identified. However, the method steps only recite measurement of binding activity. Binding is not the same as ligand or antagonist activity. Therefore, it is unclear if the claims are directed to identifying compounds that bind the EDG5 receptor or compounds that have ligand or antagonist activity.

Claim 3 is incomplete in that it refers to information in a figure. Amending the claim to refer to a sequence in the sequence listing would be remedial.

In claim 13, the recitation "isolation and purified amino acid sequence" makes no sense. It appears that "isolation" should be "isolated".

Finally, claims 13 and 14 refer to the amino acid sequence of SE QI DNO: 13. However, SEQ ID NO: 13 is a nucleotide sequence, not an amino acid sequence.

35 U.S.C. §§ 101 and 112, First Paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16, 18 and 19 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

The claims are directed to an isolated EDG5 receptor, isolated nucleotide sequences encoding same, vectors and host cells comprising the vectors, hybridization probes, and methods of screening compounds for HEDG-5 ligands or antagonists. The utility of the claimed invention rests in whether or not an EDG-5 receptor has a credible, specific and substantial utility. The specification discloses murine and human EDG-5

receptor sequences (Figure 5B for example). Based on the structural similarity of the disclosed murine and human EDG-5 receptor sequences to other receptors termed "edg" receptors in the prior art, the specification asserts that the disclosed and claimed murine and human EDG-5 receptors have EDG receptor activity. The specification also provides working examples wherein the claimed receptors respond to LPA as a ligand, and activate NF-kB.

However, the art recognizes that EDG receptors are orphan receptors, that is, their physiological significance and specific ligands are not known. See Ancellin et al. (1999, J. Biol. Chem. 274:18997-19002) who disclose that EDG-5 is one of at least three receptors that binds sphingosine 1-phosphate (SPP), and that SPP mediates a number of diverse biological responses, including increases in intracellular calcium, stimulation of fibroblast proliferation, inhibition of stress fiber formation, regulation of adhesion molecule expression and regulation of morphogenetic differentiation (p. 18997). It is not known which biological responses are induced by EDG-5. Similarly, Vogler et al. (2003, J. Invest. Dermatol. 120:693-700) disclose that there are at least five receptors that respond to SPP, including EDG-5. Vogler et al. also disclose that SPP is involved in diverse biological responses, including regulation of cell growth , differentiation, survival, and chemotaxis, as well as angiogenesis and embryogenesis (p. 693). Again, it is not known which biological responses involve EDG-5 specifically. Therefore, significant further research would be required by one skilled in the art to determine a specific utility for the claimed EDG-5 receptors, and the claimed invention lacks utility under 35 U.S.C. § 101.

Although the specification discloses that EDG-5 receptor activation leads to NF-kB activation, this also is not a specific utility. NF-kB is activated in response to many diverse stimuli, and its activation leads to many diverse biological responses. Sun et al. (2002, Shock 18 :991-06) reviews NF-kB's involvement in these responses, which include critical illness, inflammatory diseases, apoptosis, cancer, and transcriptional regulation of cytokines, adhesion molecules and other mediators (p. 99). Sun et al. state, "Further studies will be required to elucidate mechanisms regulating specificity and selectivity of NF-kB function, as well as its role in different diseases...". It is not known which biological responses involve EDG-5. Clearly then, the ability of EDG-5 to activate NF-kB is not a specific and substantial utility under 35 U.S.C. § 101.

Similarly, although the specification discloses that EDG-5 binds LPA, this is not a specific utility. LPA binds other receptors, including EDG-2 (see p. 1 of spe4cfication). LPA is involved in many diverse biological activities, reviewed in the specification at p. 11. It is not known which biological responses involve EDG-5 and thus the ability of EDG-5 to bind LPA is also not a specific and substantial utility under 35 U.S.C. § 101.

No well-established utility exists for newly isolated, complex biological molecules such as the instantly claimed EDG-5 receptors. However, the specification asserts the following as credible, specific and substantial patentable utilities for the claimed EDG-5 polypeptides:

1) to isolate new ligand(s), agonists or antagonists: This asserted utility is credible, but it is not specific, since any new protein can be used to isolate its binding

partners. Also, this asserted utility is not substantial, since significant further research would be required to determine how to use the new compounds isolated by the method.

2) in diagnostic assays for diseases associated with aberrant expression of EDG-5: The specification does not disclose a correlation between any specific disease state and altered levels or forms of EDG-5. The discovery of such a correlation involves significant research, and is an act of invention. Therefore, this asserted utility is not substantial.

3) EDG-5 nucleic acids can be used as probes, in chromosome and gene ,aping, and generation of antisense RNA: These utilities can be asserted for any new sequence and thus they are not specific for EDG-5. Furthermore, significant further research would be required to determine how to use such probes r antisense molecules, and thus this asserted utility is also not substantial.

4) EDG-5 probes can be used to identify similar sequences: This asserted utility is not specific, since any sequence can be used to identify similar sequences. Also, since the significance of such sequences is not known, further research would be required to determine how to use the similar sequences so obtained, and thus this asserted utility is also not substantial.

5) EDG-5 protein can be used to generate antibodies: This asserted utility is not specific, since any protein can be used to generate antibodies. It is also not substantial, because further research would be required to determine how to use such antibodies other than to bind EDG-5.

6) EDG-5 can be administered therapeutically to treat disease (p. 19 of specification): This asserted utility is not substantial. No correlation has been established between any specific disease state and an altered level or form of EDG-5. Therefore, significant further research would be required to identify such a disease, and determine how to treat it using EDG-5.

Claims 1-16, 18 and 19 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Please note: the effective filing date of a claimed invention is that date on which it was disclosed as having utility and being fully enabled. Since the instant claims have been rejected for both lack of utility and lack of enablement, priority to the PCT/CA98/01193document is denied, and the effective filing date for the purposes for the art rejections is the latest filing date, 12/04/2000.

Claims 1-13, 15, 16, 18 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Bandoh et al. (September 1999, J. Biol. Chem. 274:27776-27785).

Bandoh et al. teach an isolated human EDG-7 receptor and the nucleotide sequence encoding same (p. 27778, Fig. 1). It is noted that this sequence comprises a biologically active fragment of human EDG-5 or murine EDG-5 as claimed in claims 1-4 (also relevant to cl. 13). The EDG-7 is activated by LPA (re: cl. 5, see p. 27776, Abstract). The amino acid sequence disclosed in Figure 1, p. 27778, is 99.5% identical to SEQ ID NO: 14 and the nucleotide sequence would reasonably be expected to hybridize under undefined stringent conditions to SEQ ID NOS: 24 and 25 (re: cl. 6-12). Bandoh et al. teach a hybridization probe derived from the sequence (re : cl. 15, p. 27777). Bandoh et al. teach methods wherein cells expressing the receptor are contacted with compounds and tested for binding (re: cl. 16-19, p. 27777).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-16, 18 and 19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,057,126. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims are a species of the instant claims. A species renders its genus obvious.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (703) 308-2673. The examiner can normally be reached on Monday through Thursday, 6:30 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler, Ph.D. can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

ECK

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER